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EXAMINER
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KRISHNAN, GANAPATHY

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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Application Number: 10/763,377  
Filing Date: January 23, 2004  
Appellant(s): OR, YAT SUN

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Edgar W. Harlan  
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed June 22, 2009 appealing from the Office action mailed November 20, 2008.

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**(1) Real Party in Interest**

A statement identifying by name the real party in interest is contained in the brief.

**(2) Related Appeals and Interferences**

The rejection of claim 1 under 35 USC 112, first paragraph was reversed and the rejection of claims 1-12 under 35 USC 103(a) was affirmed by The Board of Patent Appeals and Interferences in its Decision on Appeal on August 25, 2008. Res Judicata and collateral estoppel may apply. MPEP 706.03(w) and 714.21 II (I).

**(3) Status of Claims**

The statement of the status of claims contained in the brief is correct.

**(4) Status of Amendments After Final**

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5) Summary of Claimed Subject Matter**

The summary of claimed subject matter contained in the brief is correct.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

**(7) Claims Appendix**

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(8) Evidence Relied Upon**

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### **(9) Grounds of Rejection**

The following ground(s) of rejection as advanced in office action of record are applicable to the appealed claims:

Claims 1-12 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Or et al (WO 99/21864), of record in the previous Office Action November 20, 2008.

Or et al teaches a process for making a bridged macrocyclic compound (formula 14, page 36) comprising the reaction of the macrocyclic compound of formula 1 (page 34, has at least two nucleophilic groups) with the bridging components  $\text{H}_2\text{N}-(\text{CH}_2)_m\text{-A-B-D-X}$  and  $(\text{CH}_2)_2\text{-C}=\text{CH}_2$  (the second bridging component with the double bond forms a pi-allyl complex with a metal; page 36, scheme 3) to yield the bridged product. The macrocyclic compound of Or is a derivative of erythromycin and is an antibiotic. The macrocyclic compound of Or (formula 1, page 34) has two sugar units attached to it. The macrocyclic compound of Or has an ethyl group attached to the carbon adjacent to the ring oxygen. This is group L in structure I in instant claim 6. It also has a second carbonyl group (at the top left of formula 1, page 34), which corresponds to X and Y in instant claim 5 taken together to form a carbonyl group.

However, Or et al teach the use of two separate bridging components to form the bridged product instead of a single bifunctional bridging component as instantly claimed. But the two individual bridging components have a functional group on one end through which the attachment to the macrocyclic compound is achieved. One of them also has a double bond, which can form a pi-allyl metal complex (as recited in instant claim 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the process of Or to make a bridged macrocyclic product as instantly claimed

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using a single bifunctional bridging component as instantly claimed since the starting material, the bridging components similar to one instantly claimed and the process steps as instantly claimed is seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to use the process of the prior art for making a bridged macrocyclic compound using a single bifunctional bridging component since the use of a single bridging bifunctional component would achieve the said bridging in two steps compared to three steps that the process of Or requires. One of ordinary skill in the art would be motivated to extend this to other macrocyclic compounds in order to develop new derivatives having improved antibacterial activity since there is a continuing need to identify new derivatives which may have less potential for developing resistance (Or, page 1, lines 15-20). One of ordinary skill in the art would also recognize that the process of making the bridged macrocyclic compound could be extended with a reasonable expectation of success to other derivatives of erythromycins since all of them have the same core structure and the required nucleophilic moieties.

#### **(10) Response to Argument**

##### **Appellants' argue that:**

1. Claim 1 was amended to recite that "each of two nucleophilic moieties of the macrocyclic compound reacts with said bifunctional bridging component." The amendment makes clear that both (of two) nucleophilic moieties of the macrocyclic compound (a single compound) involved in bridge formation react with a single bridging component. Or et al teaches macrocyclic compounds having at least two reactive groups, each of which reacts with a separate bridging component. Only after each component is attached to the macrocycle are the two

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components joined together to form a bridge. Instant claim 1 requires a single bridging component

**Examiner's Response:**

The fact that Or et al teaches macrocyclic compounds having at least two reactive groups, each of which reacts with a separate bridging component, was acknowledged in the rejection.

In Or's process (Scheme 3, page 36), it is true that the amino group in  $\text{H}_2\text{N}-(\text{CH}_2)_m-\text{A}-\text{X}^2$  reacts with the carbonyl group of the imidazole ester. The carbonyl carbon is electrophilic. This reaction is used as an extension of the bridge. In Scheme 2 at page 35, it can be seen that the imidazole ester (formula 10) is obtained via reaction of the nucleophilic hydroxyl on the macrocyclic ring with carbonyl diimidazole (page 29, lines 5-7). So, the macrocycle having a nucleophilic group is reacted with a component that becomes part of the bridge eventually. The other nucleophilic component on the macrocyclic compound is also an OH, which reacts with an allylic bromide (Or-page 27, lines 20-23) to form the  $-\text{O}-(\text{CH}_2)_n-\text{CH}=\text{CH}_2$  (this is on the right side of the macrocyclic compound in structural formula 11 at page 36). Therefore, Or's process does involve the reaction of two nucleophilic groups on the macrocycle with a bridging component.

Regarding the bridging component, claim 1 recites that it is characterized by its ability to form  $\pi$ -allyl metal complex. In formula 11 of Or, it is an allylic moiety (the second bridging component) that is attached to the oxygen. This moiety has the ability to form a  $\pi$ -allyl metal complex. This is also well known to one of ordinary skill in the art. Therefore, the macrocyclic compound and the bridging components of Or have the characteristics required by claim 1.

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Also, in Or's process both the bridging components having functional groups react with the nucleophilic groups on the macrocycle to form a covalent bond.

The only difference (which was acknowledged in the rejection of record) is that Or et al uses two bridging components having all the characteristics as required by instant claim 1, attaches them individually first and then joins them to form the bridge. The only difference in the instant process is that, the bridging component is a single moiety having all the characteristics taught by Or.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the process of Or to make a bridged macrocyclic product as instantly claimed using a single bifunctional bridging component as instantly claimed since the starting material, the bridging components similar to one instantly claimed and the process steps as instantly claimed is seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to use the process of the prior art for making a bridged macrocyclic compound using a single bifunctional bridging component since the use of a single bridging bifunctional component would achieve the said bridging in a single step (if the bridging component reacts simultaneously at both ends) or in two successive steps compared to three steps that the process of Or requires. The process is one of design by choice (using a single bridging component as opposed to using two individual bridging components) which would be recognized by one of ordinary skill in the art and is also well within the skill level of the artisan to do it. There is reasonable expectation of success.

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**Appellants' argue that:**

2. Minimizing the number of steps is one of several goals in a synthetic process. The Examiner appears to argue that the mere recognition that minimizing process steps *per se* renders obvious any process improvement that may achieve that goal. Motivation must be coupled with a suggestion of the improvement itself. There is no suggestion in Or to use a single bridging component. The Examiner's motivation without secondary evidence is incorrect.

**Examiner's Response:**

Minimizing the number of steps may be one of several goals in a synthetic process. But it is an important consideration in order to make the process efficient. Minimizing the number of steps make a process efficient by saving time and cost. Suggestion for improvement need not necessarily be expressly taught in the prior art. In the instant case, one of ordinary skill in the art looking at Or's process, especially the steps where the bridge is formed, (Scheme 3 at page 36 of Or) can and will recognize the modification of the two step bridging process using two individual bridging components to a step wherein a single bridging component is used. The only modification needed is making the bridging component single since all other structural and functional group limitations regarding the bridging components are taught by Or. When a single bridging component is used one of ordinary skill in the art will recognize that in order to carry out this particular step the macrocyclic compound and the single bridging component have to be reacted under the appropriate conditions to get the bridged product. The use of a single bridging component in the bridge forming step makes the process easier and convenient to carry out. This is something which one of skill in the art will recognize from Or's process even without secondary evidence. Secondary evidence is not needed in the instant case.



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**Appellants' argue that:**

3. The imidazole carboxylic ester moiety in Or's process is electrophilic. This is also supported by Boufi et al reference cited by the Appellants. In Or's process one of groups on the macrocyclic compound is an electrophilic group that reacts with the bridging component. Thus Or fails to teach the fundamental chemical process recited in Appellant's claims.

**Examiner's Response:**

The explanation regarding the type of groups on the macrocycle and the bridging components is explained in the response to argument #1 above. Moreover, one of ordinary skill in the art will recognize that if one group is electrophilic then the second component which reacts with it should be electrophilic and vice versa. Even if one of the groups on the macrocycle of Or is electrophilic as appellants argue, one of ordinary skill in the art can design the process step such that two nucleophilic groups on the macrocycle react with the bridging component, since the macrocyclic compound that Or starts with (structural formula 1 at page 35) has at least two nucleophilic groups on it.

The modifications pointed by the Examiner are minor modifications in the way in which a couple of steps in Or's teaching are modified. It is well within the skill level of the artisan to recognize them and use them in the process as instantly claimed with a reasonable expectation of success.

The Examiner has presented arguments above addressing this argument of the appellants.

For the reasons discussed above, it is believed that the rejections should be sustained.

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**(11) Related Proceeding(s) Appendix**

A Decision rendered by the Board in the instant case on August 25, 2008 is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

Respectfully submitted,

/Ganapathy Krishnan/  
Patent Examiner, AU 1623  
September 28, 2009

**Conferees:**

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Primary Examiner, Art Unit 1623

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